

FORM 1449\*

INFORMATION DISCLOSURE STATEMENT  
IN AN APPLICATION

(Use several sheets if necessary)

Docket Number

D0009NP;30436.53USU1

Application Number

09/877,987

Applicant

Robert M. Townsend et al.

Filing Date

June 8, 2001

Group Art Unit

1645 / 1644

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
NG	5,354,678 (Exhibit 81)	October 11, 1994	Lebkowski et al.			December 21, 1992
	5,824,655 (Exhibit 82)	October 20, 1998	Border			February 15, 1995
	6,113,898 (Exhibit 83)	September 5, 2000	Anderson et al.			June 7, 1995
	6,090,914 (Exhibit 84)	July 18, 2000	Linsley et al.			April 15, 1994

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO
	WO 98/56417 (Exhibit 85)	December 17, 1998	PCT				X
	WO 95/34320 (Exhibit 86)	December 21, 1995	PCT				X

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		Battleman, David S., et al., 1993 <i>J. Neurosci.</i> "HSV-1 Vector-Mediated Gene Transfer of the Human Nerve Growth Factor Receptor P75hNGFR Defines High-Affinity NGF Binding," 13:941-951. (Exhibit 53)
		Bolling, S.F., et al. 1996 <i>J. Surg. Res.</i> "The Time course of CTLA4Ig effect on cardiac allograft rejection," 63:320-323. (Exhibit 54)
		Bolling, S.F., et al., 1994 <i>J. Surg. Res.</i> "The Effect of combination cyclosporine and CTLA4Ig therapy on cardiac allograft survival," 57:60-64. (Exhibit 55)
		Dariavach, Piona., et al., 1988 <i>Eur. J. Immunol.</i> "Human Ig superfamily CTLA-4 gene: chromosomal localization and identity of protein sequence between murine and human CTLA-4 cytoplasmic domains," 18:1901-1905. (Exhibit 56)
		Fulmer, R.I., et al. 63 A.D. <i>The American Journal of Anatomy</i> "Transplantation of cardiac tissue into the mouse ear," 113:273-281. (Exhibit 57)
		Hansen, John A., et al., 1980 <i>Immunogenetics</i> "Monoclonal Antibodies Identifying a Novel T-Cell Antigen and Ia Antigen of Human Lymphocytes," 10:247-260. (Exhibit 58)
		Johnsson, B., et al., 1991 <i>Anal. Biochem.</i> "Immobilization of Proteins to a Carboxymethyl-dextran-Modified Gold Surface for Biospecific Interaction Analysis in Surface Plasmon Resonance Sensors," 198:268-277. (Exhibit 59)
		Khilko, S.N., et al., 1993 <i>J. Biol. Chem.</i> "Direct Detection of Major Histocompatibility Complex Class I Binding to Antigenic Peptides Using Surface Plasmon Resonance," 268:15425-15434. (Exhibit 60)
		Lauzon, R.J., et al., 1989 <i>Cell Immunol.</i> "The Role of T cell receptors in non-MHC-restricted cytotoxicity," 118:265-284. (Exhibit 61)
Ng		Carroll, R., et al., 1993 <i>Gene Therapy</i> "Construction and Characterization of Replication-Defective HIV-1 Packaging Cell", 17E:241: SZ401. (Exhibit 62)

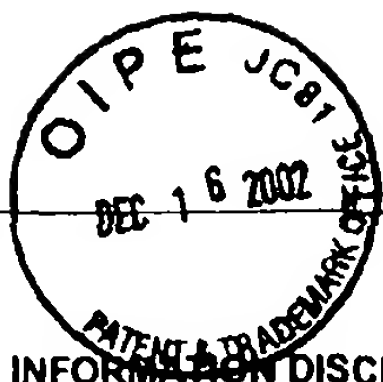
EXAMINER

G. H. P. G. M. P. 11/7/03

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

\*Substitute Disclosure Statement Form (PTO-1449) Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE



FORM 1449* <b>INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION</b>  (Use several sheets if necessary)	Docket Number D0009NP;30436.53USU1	Application Number 09/877,987
	Applicant Robert M. Townsend et al.	
	Filing Date June 8, 2001	Group Art Unit 1645/674

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
115		Linsley, Peter S., et al., 1992 <i>J. Exp. Med.</i> "Coexpression and Functional Cooperation of CTLA-4 and CD28 on Activated T Lymphocytes," 176:1595-1604. (Exhibit 63)
		Linsley, Peter S., et al., 1994 <i>Immunity</i> "Human B7-1 (CD80) and B7-2 (CD68) Bind with Similar Avidities but Distinct Kinetics to CD28 and CTLA-4 Receptors," 1:793-801. (Exhibit 64)
		Linsley, Peter S., et al., 1995 <i>J. Biol. Chem.</i> "Binding Stoichiometry of the Cytotoxic T Lymphocyte-associated Molecule-4 (CTLA-4)," 270:15417-15424. (Exhibit 65)
		Linsley, Peter S., and J.A. Ledbetter. 1993 <i>Annu. Rev. Immunol.</i> "The Role of the CD28 receptor during T cell responses to antigen," 11:191-212. (Exhibit 66)
		Malik, Najma et al., 1989 <i>Mol. and Cell. Biol.</i> "Molecular Cloning, Sequence Analysis, and Functional Expression of a Novel Growth Regulator, Oncostatin M.," 9:2847-2853. (Exhibit 67)
		Martz, E., et al. 1985 <i>Adv. Exp. Med. Biol.</i> "Lymphocyte function-associated antigens: regulation of lymphocyte adhesions in vitro and immunity in vivo," 184:291-307. (Exhibit 68)
		Metzler, William J., et al., 1997 <i>Nature Struct. Biol.</i> "Solution structure of human CTLA-4 and delineation of a CD80/CD86 Binding Site Conserved in CD28," 4:527-531. (Exhibit 69)
		O'Shannessy, et al., 1993 <i>Anal. Biochem.</i> "Determination of Rate and Equilibrium Binding Constants for Macromolecule Interactions Using Surface Plasmon Resonance: Use of Nonlinear Least Squares Analysis Methods," 212:457-468. (Exhibit 70)
		Peach, Robert J., et al., 1994 <i>J. Exp. Med.</i> "Complementarily Determining Region 1 (CDR1) and CDR3-analogous Regions in CLTA-4 and CD28 Determine the Binding to B7-1," 180:2049-2058. (Exhibit 71)
		Price, M.R., et al., 1986 <i>Br. J. Cancer</i> "Epitope analysis of monoclonal antibody NCRC-11 defined antigen isolated from human ovarian and breast carcinomas," 54:393-400. (Exhibit 72)
		Wallace, Philip M., et al., 1994 <i>Transplantation</i> "CTLA4Ig Treatment Ameliorates the lethality of murine graft-versus-host disease across major histocompatibility complex barriers," 58:602-610. (Exhibit 73)
		Williams, Sander R., et al., 1991 <i>Proc. Natl. Acad. Sci.</i> "Introduction of foreign genes into tissues of living mice by DNA-coated microprojectiles," 88:2726-2730. (Exhibit 74)
		Wingett, D., et al. 1999 <i>Cell Immunol.</i> "A Role for CD99 in T cell activation," 193:17-23. (Exhibit 75)
		Yokochi, Takashi, et al., 1982 <i>Journal of Immunology</i> "B Lymphoblast Antigen (BB-1) Expressed on Epstein-Barr Virus-Activated B Cell Blasts, B Lymphoblastoid Cell Lines, and Burkitt's Lymphomas," 128:823-827. (Exhibit 76)
		Bolling, Steven F., et al., 1996 <i>The Journal of Heart and Lung Transplantation</i> "Preventing allograft rejection with CTLA4IG: effect of donor-specific transfusion route or timing," 15:928-935. (Exhibit 77)
		Isobe, Mitsuaki, et al., 1997 <i>The Journal of Heart and Lung Transplantation</i> "Assessment of tolerance induction to cardiac allograft by anti-ICAM-1 and Anti-LFA-1 Monoclonal antibodies," 16:1149-1156. (Exhibit 78)
		Jaiswal, Archana I., et al., 1996 <i>International Immunology</i> "Regulation of CD40 ligand expression on naïve CD4 T cells: a role for TCR but not co-stimulatory signals," 8:275-285. (Exhibit 79)
		Suzuki, Jun-ichi, et al., 1997 <i>The Journal of Heart and Lung Transplantation</i> "Inhibition of accelerated coronary atherosclerosis with short-term blockade of intercellular adhesion molecule-1 and lymphocyte function-associated antigen-1 in a heterotopic murine model of heart transplantation," 16:1141-1148. (Exhibit 80)
		Greene, J., et al., 1996 <i>The Journal of Biological. Chem.</i> "Covalent Dimerization of CD28/CTLA-4 and Oligomerization of CD80/CD86 regulate T cell costimulatory interactions," 271:26762-26771. (Exhibit 87)

EXAMINER Pittman (1/7/02)	DATE CONSIDERED
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.	

<b>FORM 1449*</b>  <b>INFORMATION DISCLOSURE STATEMENT</b> <b>IN AN APPLICATION</b>  (Use several sheets if necessary)	Docket Number	Application Number
	D0009NP;30436.53USU1	09/877,987
	Applicant	
	Robert M. Townsend et al.	
	Filing Date	Group Art Unit
	June 8, 2001	1645/1647

U.S. PATENT DOCUMENTS						
EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLAS S	FILING DATE IF APPROPRIATE
PL	5,434,131 (Exhibit 154)	7/18/95	Linsley et al.			5/26/93
FOREIGN PATENT DOCUMENTS						
	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLAS S	TRANSLATION
						YES NO
	WO 95/33770 (Exhibit 124)	12/14/95	PCT			X
	WO 02/02638 A2 (Exhibit 155)	1/10/02	PCT			X
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)						
			Linsley, et al., 1991, <i>J.Exp.Med.</i> "CTLA-4 Is a Second Receptor for the B Cell Activation Antigen B7" 174:561-569. (Exhibit 88)			
			Gimmi, et al., 1993, <i>Proc.Natl.Acad.Sci. USA</i> "Human T-Cell clonal anergy is induced by antigen presentation in the absence of B7 costimulation" 90:6586-6590. (Exhibit 89)			
			Azuma et al., 1993 <i>Nature</i> "B70 antigen is a second ligand for CTLA-4 and CD28" 366:76-79. (Exhibit 90)			
			Ronchese et al., 1994 <i>J.Exp.Med</i> "Mice Transgenic for a Soluble Form of Murine CTLA-4 Show Enhanced Expansion of Antigen-specific CD4 T Cells and Defective Antibody production In Vivo" 179:809-817. (Exhibit 91)			
			Griggs et al., 1996 <i>J.Exp.Med</i> "The Relative Contribution of the CD28 and gp39 Costimulatory pathways in the Clonal Expansion and Pathgenic Acquisition of Self-reactive T Cells" 183:801-810. (Exhibit 92)			
			Verwilghen et al., 1994 <i>J-Immunol.</i> Expression of Functional B& and CTLA4 on Rheumatoid Synovial T Cells" 153:1378-1385. (Exhibit 93)			
			Blazar et al., 1994 <i>Blood</i> "In Vivo Blockade of CD28/CTLA4: Interaction With CTLA4-Ig Reduces Lethal Murine Graft-Versus-Host Disease Across the Major Histocompatibility Complex Barrier in Mice" 83:3815-3825. (Exhibit 94)			
			Finck et al., <i>Science</i> "Treatment of Murine lupus with CTLA4Ig" 265:1225-1227. (Exhibit 95)			
			Perrin et al., 1995 <i>J-Immunol</i> "Role of B7:CD28/CTLA4 in the Induction of Chronic Relapsing Experimental Allergic Encephalomyelitis" 154:1481-1490. (Exhibit 96)			
			Pearson et al., 1994 <i>Transplantation</i> "Transplantation Tolerance Induced By CTLA4-Ig" 57:1701-1706. (Exhibit 97)			
			Baliga et al., 1994 <i>Transplantation</i> "CTLA4Ig PROLONGS ALLOGRAFT SURVIVAL WHILE SUPPRESSING CELL-MEDIATED IMMUNITY" 58:1082-1090. (Exhibit 98)			
ML			Tepper et al., 1994 <i>Transplantation Proceedings</i> "Tolerance Induction by soluble CTLA4 in a Mouse Skin Transplant Model" 26:3151-3154. (Exhibit 99)			

EXAMINER	Patricia L. M. 11/7/03	DATE CONSIDERED
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.		

\*Substitute Disclosure Statement Form (PTO-1449) Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FORM 1449*	Docket Number	Application Number
	D0009NP;30436.53USU1	09/877,987
	Applicant	
	Robert M. Townsend et al.	
INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION	Filing Date	Group Art Unit
	June 8, 2001	1645 1644
(Use several sheets if necessary)		

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
M		Perico et al., 1995 <i>Kidney International</i> "Toward novel antirejection strategies: In vivo immunosuppressive properties of CTLA4Ig" 47:241-246. (Exhibit 100)
		Finck et al., 1994 <i>Arthritis and Rheumatism</i> "Effects of CTLA4Ig in murine lupus" 37:S222. (Exhibit 101)
		Nishikawa et al., 1994 <i>Eur J. Immunol.</i> "Effect of CTLA-4 chimeric protein on rat autoimmune anti-glomerular basement membrane glomerulonephritis" 24:1249-1254. (Exhibit 102)
		Wallace et al., 1994 <i>Transplantation</i> "CTLA4Ig treatment ameliorates the lethality of murine graft-versus-host disease across major histocompatibility complex barriers" 58:602-610. (Exhibit 103)
		Damle et al., <i>J. Immunol.</i> "Costimulation of T Lymphocytes with integrin Ligands intercellular Adhesion Molecule-1 or Vascular Cell Adhesion Molecule-1 Induces Functional Expression of CTLA-4, a Second Receptor for B7" 152:2686-2697. (Exhibit 104)
		Milich, et al., 1994 <i>J. Immunol</i> "Soluble CTLA-4 can suppress autoantibody production and elicit long term unresponsiveness in a novel transgenic model," 153:429-435. (Exhibit 105)
		Webb, et al., 1996 <i>Eur J. Immunol</i> "Prevention and amelioration of collagen-induced arthritis by blockade of the CD28 co-stimulatory pathway: requirement for both B7-1 and B7-2," 26:2320-2328. (Exhibit 106)
		Van Oosterhout, et al., 1997 <i>Am.J Respir. Cell Mol. Biol.</i> "Murine CTLA4-IgG Treatment Inhibits Airway Eosinophilia and Hyperresponsiveness and Attenuates IgE Upregulation in a Murine Model of allergic Asthma," 17:386-392. (Exhibit 107)
		Abrams et al., 1999 <i>J-Clin-Invest</i> "CTLA4Ig-mediated blockade of T-cell costimulation in patients with psoriasis vulgaris. 103:1243-1252. (Exhibit 108)
		Ibrahim, et al., 1996 <i>Blood</i> "CTLA4Ig Inhibits Alloantibody Responses to Repeated Blood Transfusions," 88:4594-4600. (Exhibit 109)
		Lenschow, et al., 1995 <i>J Exp Med</i> "Differential Effects of anti-B7-1 and Anti-b&-2 Monoclonal Antibody Treatment on the Development of Diabetes in the Nonobese Diabetic Mouse," 181:1145-1155. (Exhibit 110)
		Lenschow, et al., 1992 <i>Science</i> "Long-Term Survival of Xenogeneic Pancreatic islet Grafts Induced by CTLA4Ig," 257:789-792. (Exhibit 111)
		Sayegh, 1999 <i>J Clin Invest</i> "Finally, CTLA4Ig graduates to the clinic," 103:1223-1225. (Exhibit 112)
		Wolfe, 1995 <i>Bailliere's Clinical Rheumatology</i> "The epidemiology of drug treatment failure in rheumatoid arthritis," 9:619-632. (Exhibit 113)
		Hochberg, et al., 1990 <i>Epidemiologic Reviews</i> "Epidemiology of Rheumatoid Arthritis: Update," 12:247-252. (Exhibit 114)
		Spector, 1990 <i>Epidemiology of Rheumatic Disease</i> "Rheumatoid Arthritis," 16:513-537. (Exhibit 115)
		Liu MF, Kohsaka H Sakurai H, Azuma m Okumura K Saito I, Miyasaka N, 1996. "The presence of costimulatory molecules B7.1 (CD80) and B7.2 (CD86) in rheumatoid arthritis synovium" <i>Arthritis-Rheum.</i> Jan; 39(1): 110-4. (Exhibit 116)
		Sfikakis PP, Via CS. 1997 "Expression of CD28, CTLA4, CD80, CD86 molecules in-patients with autoimmune rheumatic diseases: implications for immunotherapy". <i>Clin-Immunol-Immunopathol.</i> Jun; 83(3): 195-8. (Exhibit 117)
M		Sayegh MH, Akalin E, Hancock WW, Russell ME, Carpenter CB, Linsley PS, Turka LA, 1995. <i>J. Exp. Med.</i> "CD28-B7 blockade after all antigenic challenge in vivo inhibits Th1 cytokines but spares Th2". 181: 1869-1874. (Exhibit 118)

EXAMINER	PHURD G. M. 11/2/03	DATE CONSIDERED
----------	---------------------	-----------------

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.



<b>FORM 1449*</b>  <b>INFORMATION DISCLOSURE STATEMENT</b> <b>IN AN APPLICATION</b>  (Use several sheets if necessary)	Docket Number	Application Number
	D0009NP;30436.53USU1	09/877,987
	Applicant	
	Robert M. Townsend et al.	
	Filing Date	Group Art Unit
	June 8, 2001	1645 / 1644

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
<i>MU</i>		Racusen LC; et. al. 1999. "The Baniff 97 working classification of renal allograft pathology". <i>Kidney-Int.</i> 55(2): 713- 723. (Exhibit 119)
		Parkin D, Jacoby A, McNamee P, 2000. "Treatment of multiple sclerosis with interferon $\beta$ : an appraisal of cost-effectiveness and quality of life" <i>J Neurol Neurosurg Psychiatry</i> ; 68: 144-149. (Exhibit 120)
		Nortvedt MW, Riise T, Myhr KM, and Nyland HI, 1999. "Quality of life in multiple sclerosis: measuring the disease effects more broadly" <i>Neurology</i> ; 53(5): 1098-1103 (Exhibit 121)
		Pearson TC, Alexander DZ, Winn KJ, Linsley PS, Lowry RP, Larsen CP, 1994. "Transplantation tolerance induced by CTLA4-Ig. <i>Transplantation</i> , 57:1701-1706. (Exhibit 122)
		Liao HX, Haynes BF, 1995. "Role of adhesion molecules in the pathogenesis of rheumatoid arthritis" <i>Rheum-Dis-Clin-Noth-Am.</i> Aug; 21(3): 715-40. (Exhibit 123)
		Thomas R, Quinn C. 1996. "Functional differentiation of dendritic cells in rheumatoid arthritis: role of CD86 in the synovium" <i>J-Immunol.</i> Apr 15; 156(8): 3074-86. (Exhibit 125)
		Verhoeven-AC; Boers-M; Tugwell-P, 1998. "Combination therapy in rheumatoid arthritis: updated systematic review" <i>Br-J-Rheumatol.</i> Jun;37 (6): 612-619 (Exhibit 126)
		Schiff M, 1997. "Emerging treatments for rheumatoid arthritis" <i>Am-J-Med.</i> Jan 27; 102 (1A): 11S-15S (Exhibit 127)
		Balsa A, Dixey J, Sansom DM, Maddison PJ, Hall ND, 1996. "Differential expression of the costimulatory molecules B7.1 (CD80) and B7.2 (CD86) in rheumatoid synovial tissue" <i>Br-J-Rheumatol.</i> Jan; 35(1): 33-7 (Exhibit 128)
		Ranheim Ea, Kipps Tj, 1994. "Elevated expression of CD80 (B7/BB1) and other accessory molecules on synovial fluid mononuclear cell subsets in rheumatoid arthritis" <i>Arthritis-Rheum.</i> Nov;37 (11): 1637-1647 (Exhibit 129)
		Freeman, GJ, Gribben JG, Boussiotis VA, et. al. 1993. "Cloning of B7-2: a CTLA-4 counter receptor that costimulates human T cell proliferation" <i>Science</i> , 262: 909-911. (Exhibit 130)
		Becker, J.C., March 8, 2001, Abstract and of Presentation of "A multi-center, randomized, double-blind, placebo controlled study to evaluate the safety and preliminary clinical activity of multiple doses of CTLA4Ig and LEA29Y administration intravenously to subjects with rheumatoid arthritis," presented at American College of Rheumatology Conference: "2001 Innovative Therapies in Autoimmune Diseases," San Francisco, California (Exhibit 131)
		Aruffo, S., March 27, 2000, Presentation of "Approaches to Immune Regulation" at BIO 2000 in Boston, Mass. (Exhibit 132)
		Abrams, et al., September 4, 2000, <i>J.Exp.Med.</i> "Blockade of T Lymphocyte Costimulation with Cytotoxic T Lymphocyte- associated Antigen 4-Immunoglobulin (CTLA4Ig) Reverse the Cellular Pathology of Psoriatic plaques, Including the Activation of Keratinocytes, Dendritic Cells, and Endothelial Cells," 192:681-693. (Exhibit 133)
		Srinivas, N.R. et al., December 1, 1995, <i>J.Pharmaceutical Sciences</i> "Pharmacokinetics and pharmacodynamics of CTLA4Ig (BMA-188667), a Novel Immunosuppressive Agent, in Monkeys following Multiple Doses," 85:1-4. (Exhibit 134)
		Gandhi, et al., November 18, 1998, Abstract and Presentation of <i>PharmSci Supplement</i> "Physical and Chemical Characterization of BMS-224818, A Recombinant Fusion Protein," in San Francisco, Ca. (Exhibit 135)
		Flesher, A.R., April 15, 1999, <i>Biological Process Sciences</i> Presentation of "Transgenic Production, A Comparative Study" at Bio 99 in Seattle, Washington. (Exhibit 136)
<i>M</i>		Greve, K.F., May 9, 1996, <i>J Chromatography</i> "Capillary electrophoretic examination of underivatized oligosaccharide mixtures released from immunoglobulin G antibodies and CTLA4Ig fusion protein," 749:237-245. (Exhibit 137)

EXAMINER

*P. W. P. G. M. 11/17/03*

DATE CONSIDERED

EXAMINER: Initial if reference considered, wh ther or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for n xt communication to the Applicant.

\*Substitute Disclosure Statement Form (PTO-1449) Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

<b>FORM 1449*</b>  <b>INFORMATION DISCLOSURE STATEMENT</b> <b>IN AN APPLICATION</b>  (Use several sheets if necessary)	Docket Number	Application Number
	D0009NP;30436.53USU1	09/877,987
	Applicant	
	Robert M. Townsend et al.	
	Filing Date	Group Art Unit
	June 8, 2001	1645 <i>1644</i>

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
<i>MS</i>		Srinivas, N.R., April 8, 1997, <i>Pharmaceutical Research</i> "Assessment of Dose Proportionality, Absolute Bioavailability, and Immunogenicity Response of CTLA4g (BMS-188667), a Novel Immunosuppressive Agent, Following Subcutaneous and Intravenous Administration to Rats," 14:911-916. (Exhibit 138)
		Weiner, R.S., November 6-10, 1994, Abstract and Presentation of "Validation and PK Application of a Double Antibody Sandwich Enzyme Immunoassay For the Quantitation of Human CTLA4g Fusion Protein (BMS-188667) In Mouse Serum," (Exhibit 139)
		Weiner, R.S., June 6, 1996, <i>J Pharmaceutical and Biomedical Analysis</i> "A sensitive enzyme immunoassay for the quantitation of human CTLA4g fusion protein in mouse serum: pharmacokinetic application to optimizing cell line selection," 15:571-579. (Exhibit 140)
		Warner, G.I. et al., March 16-22, 1995, Abstract and Presentation of "Bioactivity of BMS-188667 (CTLA4g) in Cynomolgus Monkeys," in Seattle, Washington. (Exhibit 141)
		Weiner, R.S., March 1, 2000, Abstract and Presentation of "Industrial Perspectives of Primary Analytical Tools for Macromolecules- Principles and Applications with Examples." (Exhibit 142)
		Weiner, R.S., November 1995 Abstract and Presentation of "Validation of an Enzyme Immunoassay For The Quantitation of Human CTLA4g Fusion Protein In Human Serum," in Miami, Florida. (Exhibit 143)
		Weiner, R.S., November 1995 Abstract and Presentation of "Automation and Validation of An EIA For Quantitation of Human CTLA4g In Monkey Serum," in Miami, Florida. (Exhibit 144)
		Webb, L.M.C. et al., July 23, 1996 <i>Eur J Immunol</i> "Prevention and amelioration of collagen-induced arthritis by blockade of the CE28 co-stimulatory pathway: requirement for both B7-1 and B7-2" 26:2320-2328. (Exhibit 145)
		Knoerzer, et al., May 5, 1995, <i>J Clin. Invest</i> "Collagen-induced Arthritis in the BB Rat Prevention of Disease by Treatment with CTLA4g" 96:987-993. (Exhibit 146)
		Larsen, et al., April 27, 2000, Abstract of "Prolongation of Renal Allograft Survival with Blockade of the CD28 Pathway Using A Novel Mutant CTLA4-Ig Fusion Protein In Non-Human Primates," in <i>Transplantation</i> , 69(8):#44, p. S123, Chicago, IL. (Exhibit 147)
		Larsen, et al., May 13-17, 2000, A Presentation of "Prolongation of Renal Allograft Survival With Blockade of the CD28 Pathway Using A Novel Mutant CTLA4-Ig Protein In Nonhuman Primates" at the American Society of Transplantation Meeting in Chicago, IL. (Exhibit 148)
		Larsen, Aug. 27-Sept. 1, 2000, A Presentation of "Manipulation of Costimulatory Pathways: Targeting CD80 and CD86" at the XVII congress of the Transplantation Society in Rome, Italy. (Exhibit 149)
		Larsen, March 3-4, 2000, A Presentation of "Costimulation blockade: progress toward clinical application" at Canadian Society of Transplantation Annual Scientific meeting in Mont Tremblant, Quebec, Canada. (Exhibit 150)
		Larsen, Jan. 13-17, 2000, A Presentation of "Costimulation blockade: Progress toward clinical application" at the American Society of Transplantation Meeting in Las Croabas, Puerto Rico. (Exhibit 151)
		Hathcock, et al., August 30, 1993 <i>Science</i> "Identification of an Alternative CTLA-4 Ligand Costimulatory for t Cell Activation," 262:905-911. (Exhibit 152)
<i>MS</i>		Sfikakis, et al., November 29, 1994 <i>Arthritis &amp; Rheumatism</i> "CD28 Expression On T Cell Subsets in Vivo And CD28-Mediated T Cell Response In Vitro In Patients With Rheumatoid Arthritis," 38:649-654. (Exhibit 153)

EXAMINER <i>JHL up 6/11/03</i>	DATE CONSIDERED
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.	

<b>FORM 1449*</b>  <b>INFORMATION DISCLOSURE STATEMENT</b> <b>IN AN APPLICATION</b>  (Use several sheets if necessary)	Docket Number	Application Number
	D0009NP;30436.53USU1	09/877,987
	Applicant	
	Robert M. Townsend et al.	
	Filing Date	Group Art Unit
	June 8, 2001	1645 <i>1644</i>

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
<i>ms</i>		Lakkis, Fadi G., et al., "Blocking the CD28-B7 T Cell Costimulation Pathway Induces Long Term Cardiac Allograft Acceptance in the Absence of IL-4 <sup>1</sup> ," <i>The Journal of Immunology</i> , 1997, 158:2443-2448. (Exhibit 156)
		Pearson, Thomas C., et al., "ANALYSIS OF THE B7 COSTIMULATORY PATHWAY IN ALLOGRAFT REJECTION <sup>1</sup> ," <i>Transplantation</i> , 1997, 63:1463-1469. (Exhibit 157)
		Pearson, Thomas C., et al., "TRANSPLANTATION TOLERANCE INDUCED BY CTLA4-Ig <sup>1</sup> ," <i>Transplantation</i> , 1994, 57:1701-1706. (Exhibit 158)
		Alexander, Diane Z., "ANALYSIS OF A FUNCTIONAL ROLE FOR CHIMERISM IN CTLA4-Ig PLUS BONE MARROW-TREATED CARDIAC ALLOGRAFT RECIPIENTS," <i>Transplantation</i> , 1994, 91:416-418. (Exhibit 159)
		Larsen, Christian P., et al., "CD40-gp39 INTERACTIONS PLAY A CRITICAL ROLE DURING ALLOFRAFT REJECTION" <i>Transplantation</i> , 1996, 61:4-9. (Exhibit 160)
		Pearson, Thomas C., et al., "CTLA4-Ig PLUS BONE MARROW INDUCES LONG-TERM ALLOGRAFT SURVIVAL AND DONOR-SPECIFIC UNRESONSIVENESS IN THE MURINE MODEL", <i>Transplantation</i> , 1996, 61:997-1004. (Exhibit 161)
		Weber, C.J., et al., "CTLA4-Ig Prolongs Survival of Microencapsulated Rabbit Islet Xenografts in Spontaneously Diabetic Nod Mice," <i>Transplantation Proceedings</i> , 1996, 28:821-823. (Exhibit 162)
		Alexander, D.Z., et al., "Analysis of effector mechanisms in murine cardiac allograft rejection," <i>Transplantation Immunology</i> , 1996, 4:46-48. (Exhibit 163)
		Larsen, Christian P., et al., "Long-Term acceptance of skin and cardiac allografts after blocking CD40 and CD28 pathways," <i>Nature</i> , 1996, 381:434-438. (Exhibit 164)
		Elwood, Eric T., et al., "Microchimerism and rejection in clinical transplantation," <i>The Lancet</i> , 1997, 349:1358-1360. (Exhibit 165)
		Larsen, Christian P., and Thomas C. Pearson, "The CD40 pathway in allograft rejection, acceptance, and tolerance," <i>Transplantation</i> , 1997, 9:641-647. (Exhibit 166)
		Konieczny, Bogumila T., et al., "IFN-γ Critical for Long-Term Allograft Survival Induced by Blocking the CD28 and CD40 Ligand T Cell Constimulation Pathways <sup>1</sup> ," <i>The Journal of Immunology</i> , 1998, 160:2059-2064. (Exhibit 167)
		Elwood, Eric T., et al., "PROLONGED ACCEPTANCE OF CONCORDANT AND DISCORDANT XENOGRAFTS WITH COMBINED CD40 AND CD28 PATHWAY BLOCKADE <sup>1</sup> ," <i>Transplantation</i> , 1998, 65:1422-1428. (Exhibit 168)
		Niimi, Masanori, et al., "The Role of the CD40 Pathway in Alloantigen-Induced Hyporesponsiveness in Vivo <sup>1</sup> ," <i>The Journal of Immunology</i> , 1998, 161:5331-5337. (Exhibit 169)
		Whitmire, Jason K., et al., "CD40-CD40 Ligand Costimulation Is Required for Generating Antiviral CD4 T Cell Responses But is Dispensable for CD8 T Cell Responses <sup>1</sup> ," <i>The Journal of Immunology</i> , 1999, 163:3194-3201. (Exhibit 170)
		Bingaman, Adam W., et al., "Vigorous Allograft Rejection in the Absence of Danger <sup>1</sup> ," <i>Journal of Immunology</i> , 2000, 164:3065-3071. (Exhibit 171)
<i>ms</i>		Bingaman, Adam W., et al., "TRANSPLANTATION OF THE BONE MARROW MICROENVIRONMENT LEADS TO HEMATOPPIETIC CHIMERISM WITHOUT CYTOREDUCTIVE CONDITIONING," <i>Transplantation</i> , 2000, 69:2491-2496. (Exhibit 172)

EXAMINER

*Plu... 11/17/03*

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

\*Substitute Disclosure Statement Form (PTO-1449) Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FORM 1449*	Docket Number	Application Number
	D0009NP;30436.53USU1	09/877,987
	Applicant	
	Robert M. Townsend et al.	
INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION	Filing Date	Group Art Unit
	June 8, 2001	1645/1647
(Use several sheets if necessary)		

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
M		Durham, Megan M., et al., "Cutting Edge: Administration of Anti-CD40 Ligand and Donor Bone Marrow Leads to Hemopoietic Chimerism and Donor-Specific Tolerance Without Cytoablative Conditioning <sup>1</sup> ," <i>Cutting Edge</i> , 2000, 165:1-4. (Exhibit 173)
		Williams, Matthew A., et al., "Genetic Characterization of Strain Differences in the Ability to Mediate CD40/CD28-Independent Rejection of Skin Allografts <sup>1</sup> ," <i>The Journal of Immunology</i> , 2000, 165: 6549-6857. (Exhibit 174)
		Bingaman, Adam W., et al., "The role of CD40L in T cell-dependent nitric oxide production by murine macrophages," <i>Transplant Immunology</i> , 2000, 8:195-202. (Exhibit 175)
		Adams, Andrew B., et al., "Costimulation Blockade, Busulfan, and Bone Marrow Promote Titratable Macrochimerism, Induce Transplantation Tolerance, and Correct Genetic Hemoglobinopathies with Minimal Myelosuppression <sup>1</sup> ," <i>The Journal of Immunology</i> , 2001, 167:1103-1111. (Exhibit 176)
		Meng, L., "Blockade of the CD40 Pathway Fails to Prevent CD8 T Cell-Mediated Intestinal Allograft Rejection," <i>Transplantation Proceedings</i> , 2001, 33:418-420. (Exhibit 177)
		Guo, Zhong., et al., "CD8 T CELL-MEDIATED REJECTION OF INTESTINAL ALLOGRAFTS IS RESISTANT TO INHIBITION OF THE CD40/CD154 COSTIMULATORY PATHWAY," <i>Transplantation</i> , 2001, 71:1351-1354. (Exhibit 178)
		Ha, Jongwon., et al., "Aggressive skin allograft rejection in CD28 <sup>-/-</sup> mice independent of the CD40/CD40L costimulatory pathway," <i>Transplant Immunology</i> , 2001, 9:13-17. (Exhibit 179)
		Bingaman, Adam W., et al., "ANALYSIS OF THE CD40 AND CD28 PATHWAYS ON ALLOIMMUNE RESPONSES BY CD4 <sup>+</sup> T CELLS IN VIVO <sup>1</sup> ," <i>Transplantation</i> , 2001, 72:1286-1292. (Exhibit 180)
		Adams, Andrew B., et al., "Calcineurin Inhibitor- Free CD28 Blockade-Based Protocol Protects Allogeneic Islets in Nonhuman Primates," <i>Diabetes</i> , 2002, 51:265-270. (Exhibit 181)
		Whelchel, JD., et al. "Evolving Strategies in immunosuppressive Therapy: The Emory Experience," <i>Clinical Transplants</i> , 1996, 20:249-255 (Exhibit 182)
		Ritichie, SC., et al., "Regulation of Immunostimulatory function and B7 molecule expression on murine dendritic cells," <i>Journal of Cellular Biochemistry</i> , 1995, 21A:C1-215 (Exhibit 183)
		Alexander, DZ., et al., "Analysis of the mechanisms of CTLA4-Ig plus bone marrow induced transplantation tolerance," <i>Journal of Cellular Biochemistry</i> , 1995, 21A:C1-301 (Exhibit 184)
		Alexander, DZ., et al., "CTLA4-Ig induced transplantation tolerance: analysis of donor cell chimerism," <i>Surgical Forum</i> , 1994, 45:402-403 (Exhibit 185)
		Pearson, TC., et al., "CTLA4-Ig plus bone marrow induces transplantation tolerance in the murine model," <i>Journal of Cellular Biochemistry</i> , 1995, 21A:C1-327 (Exhibit 186)
		Lakkis, FG., et al., "CTLA4Ig induces long-term cardiac allograft survival in the absence of interleukin-4," <i>Journal of the American Society of Nephrology</i> , 1996, 7:A3204 (Exhibit 187)
		L104EA29Y (Figure 6 of the subject application) was provided to researchers at Emory University, subject to use restrictions and confidentiality by agreement, more than one year before the priority date of the subject application, i.e. May 26, 2000, for use in animal studies in the U.S.
M		L104EA29Y (Figure 6 of the subject application) has been the subject of human clinical trials under the direction and control of Bristol-Myers Squibb Company. L104EA29Y was given to investigators who were involved in the clinical trials subject to use restrictions and confidentiality by agreement. L104EA29Y was administered intravenously to human patients in clinical trials.

EXAMINER	PHILIP C. MAGEE 11/17/03	DATE CONSIDERED
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.		



<b>FORM 1449*</b>  <b>INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION</b>  (Use several sheets if necessary)	Docket Number	Application Number
	D0009NP;30436.53USU1	09/877,987
	Applicant	
	Robert M. Townsend et al.	
	Filing Date	Group Art Unit
	June 8, 2001	1645/6 M

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
Mu		L104EA29Y was first administered intravenously to a human patient as early as November 30, 1998 in Scotland.
		L104EA29Y was first administered intravenously to a human patient as early as April 24, 1999 in the United States.
		A letter dated July 9, 1998 including a report, submitted to the U.S. Food and Drug Administration in connection with an Investigational New Drug (IND) application, is enclosed as Exhibit 188.
		The letter and report are confidential and were provided confidentially, pursuant to 21 C.F.R. §20.111 or §21 C.F.R. §312.120, to the Center for Biologics Evaluation and Research at the U.S. Food and Drug Administration in connection with the Investigational New Drug Application.
		The enclosed letter and report are redacted versions of what were sent to the U.S. Food and Drug Administration.
		The report contained the sequence for BMS-224818 (Figure 3 at page 13 of Exhibit 171), which differs from CTLA4Ig at two amino acid residues, Leu104-Glu and Ala29-Tyr (Exhibit 171 at page 2).
		An Investigator Brochure dated January 26, 1999 is enclosed as Exhibit 189.
		The Investigator Brochure is confidential and was provided to investigators who were involved in the clinical trials and subject to confidentiality by agreement, more than one year before the priority date of the subject application, i.e. May 26, 2000.
		The enclosed Investigator Brochure is a redacted version of what was sent to investigators.
Mu		The Investigator Brochure contained a text description and a schematic representation of LEA29Y (Figure 1 at page 6 of Exhibit 172), but not the sequence of L104EA29Y (Figure 6, of the subject application).

EXAMINER	PHUMP 61 W.202 11/17/03	DATE CONSIDERED
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.		

FORM 1449\*

Docket Number

D0009NP;30436.53USU1

Application Number

09/877,987

**INFORMATION DISCLOSURE STATEMENT  
IN AN APPLICATION**

(Use several sheets if necessary)

Applicant

Robert M. Townsend et al.

Filing Date

June 8, 2001

Group Art Unit

1645

61644

**U.S. PATENT DOCUMENTS**

EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
<i>ME</i>	6,444,792 (Exhibit 197)	September 3, 2002	Gray et al.			
	5,968,510 (Exhibit 206)	October 10, 1999	Linsley et al.			
	5,844,095 (Exhibit 207)	December 1, 1998	Linsley et al.			
	5,851,795 (Exhibit 218)	December 22, 1998	Linsley et al.			
	5,958,403 (Exhibit 219)	September 28, 1999	Strom et al.			
	5,770,197 (Exhibit 223)	June 23, 1998	Linsley et al.			
	6,132,992 (Exhibit 224)	October 17, 2000	Ledbetter et al.			
	5,773,253 (Exhibit 225)	June 30, 1998	Linsley et al.			
	5,885,796 (Exhibit 226)	March 23, 1999	Linsley et al.			
	5,977,318 (Exhibit 227)	November 2, 1999	Chou			
	5,885,579 (Exhibit 228)	March 23, 1999	Linsley et al.			
	5,993,800 (Exhibit 229)	November 30, 1999	Linsley et al.			
	5,916,560 (Exhibit 230)	June 29, 1999	Larsen et al.			
	5,637,481 (Exhibit 232)	June 10, 1997	Ledbetter et al.			

**FOREIGN PATENT DOCUMENTS**

	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO
	WO 01/90122 A2 (Exhibit 190)	November 29, 2001	PCT				
	WO 01/54732 A1 (Exhibit 191)	August 2, 2001	PCT				
	WO 00/23115 (Exhibit 192)	April 27, 2000	PCT				

EXAMINER

*PTA/NE/MA/2 1/17/03*

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

\*Substitute Disclosure Statement Form (PTO-1449) Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FORM 1449\*

Docket Number

Application Number

D0009NP;30436.53USU1

09/877,987

Applicant

Robert M. Townsend et al.

Filing Date

June 8, 2001

Group Art Unit

1645

# INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION

(Use several sheets if necessary)



RECEIVED  
JUN 19 2003  
TECH CENTER 1600/290

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO
M	WO 97/28267 (Exhibit 193)	August 7, 1997	PCT				
	WO 96/14865 (Exhibit 194)	May 23, 1996	PCT				
	WO 98/31820 (Exhibit 195)	July 23, 1998	PCT				
	WO 94/28912 (Exhibit 196)	December 22, 1994	PCT				
	WO 93/19767 (Exhibit 198)	October 14, 1993	PCT				
	WO 94/29436 (Exhibit 199)	December 22, 1994	PCT				
	WO 95/33823 (Exhibit 200)	December 14, 1995	PCT				
	WO 93/00431 (Exhibit 201)	January 7, 1993	PCT				
	EP 0 613 944 A2 (Exhibit 202)	September 7, 1994	EP				
	EP 0 682 039 A1 (Exhibit 203)	November 15, 1995	EP				
	WO 01/92337 (Exhibit 208)	December 6, 2001	PCT				
	WO 98/33,513 (Exhibit 217)	August 6, 1998.	PCT				

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Morton, Phillip A. et al., "Differential Effects of CTLA-4 Substitutions on the Binding of Human CD80 (B7-1) and CD86 (B7-2)," <i>Journal of Immunology</i> , 1996, 156:1047-1054 (Exhibit 204)
	Souza, D. et al., "Synergistic Inhibition of Established Collagen Induced Arthritis (CIA) Through Dual Inhibition of ICAM-1 and CD40L Pathways," <i>Arthritis and Rheumatism</i> , 1999, 42:S60 (Exhibit 205)
	Alegre, Maria-Luisa et al., "Immunomodulation of Transplant Rejection Using Monoclonal Antibodies and Soluble Receptors," <i>Digestive Diseases and Sciences</i> , 1995, 40:58-64 (Exhibit 209)
	Murakami, Masaaki et al., "Identification and characterization of an alternative cytotoxic T lymphocyte-associated protein 4 binding molecule on B cells," <i>Proceedings of the National Academy of Sciences USA</i> , 1995, 93:7838-7842 (Exhibit 210)
M	Peach, Robert J. et al., "Both Extracellular Immunoglobulin-like Domains of CD80 Contain Residues Critical for Binding T Cell Surface Receptors CTLA-4 and CD28," <i>Journal of Biological Chemistry</i> , 1995, 270:21181-21187. (Exhibit 211)

EXAMINER

Philly Granger 11/17/03

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

\*Substitute Disclosure Statement Form (PTO-1449) Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

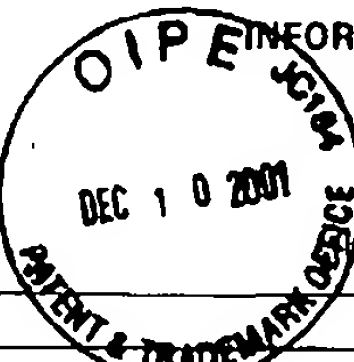
**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, Etc.)

**EXAMINER**

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.



<b>FORM 1449*</b>  	<b>INFORMATION DISCLOSURE STATEMENT IN AN APPLICATION</b>  (Use several sheets if necessary)	<b>Docket Number</b> D0009NP/30436.53USU1	<b>Application Number</b> 09/877,987
		<b>Applicant</b> Robert M. Townsend et al.	
	<b>Filing Date</b> June 8, 2001	<b>Group Art Unit</b> 1645 / 1645	

U.S. PATENT DOCUMENTS						
EXAMINER INITIAL	DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
FOREIGN PATENT DOCUMENTS						
	DOCUMENT NO.	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO
	WO95/33770 (Exhibit 1)	December 14, 1995	CDM E-2000			
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)						
M6		Armitage, Richard J. et al., "Molecular and Biological Characterization of a Murine Ligand for CD40," <i>Letters to Nature</i> , May 7, 1992, 357:80-2. (Exhibit 2)				
		Aruffo, Alejandro and Brian Seed, "Molecular Cloning of a CD28 cDNA by a High-Efficiency COS Cell Expression System," <i>Proc. Nat'l Acad. Sci., USA</i> , December 1987, 84:8573-7. (Exhibit 3)				
		Azuma, Haruhito et al., "Blockade of T-Cell Costimulation Prevents Development of Experimental Chronic Renal Allograft Rejection," <i>Proc. Nat'l. Sci. Acad. USA</i> , October 1996, 93:12439-44. (Exhibit 4)				
		Blazar, Bruce R. et al., "Coblockade of the LFA1:ICAM and CD28/CTLA4:B7 Pathways Is A Highly Effective Means of Preventing Acute Lethal Graft-Versus-Host Disease Induced by Fully Major Histocompatibility Complex-Disparate Donor Grafts," <i>Blood</i> , May 1, 1995, 85(9):2607-18. (Exhibit 5)				
		Brunet, Jean-François et al., "A New Member of the Immunoglobulin Superfamily-CTLA-4," <i>Nature</i> , July 16, 1987, 328:267-70. (Exhibit 6)				
		Ciubotariu, Rodica et al., "Specific Suppression of Human CD4 <sup>+</sup> Th Cell Responses to Pig MHC Antigens by CD28 <sup>+</sup> CD28 <sup>-</sup> Regulatory T Cells," <i>The American Association of Immunologists</i> , 1998, 161:5193-5202. (Exhibit 7)				
		Daikh, David et al., "The CD28-B7 Costimulatory Pathway and Its Role in Autoimmune Disease," <i>Journal of Leukocyte Biology</i> , August 1997, 62:156-62. (Exhibit 8)				
		Damle, Nitin K. et al., "Costimulation of T Lymphocytes with Integrin Ligands Intercellular Adhesion Molecule-1 or Vascular Cell Adhesion Molecule-1 Induces Functional Expression of CTLA-4, a Second Receptor for B7," <i>Journal of Immunology</i> , 1994, 152:2686-97. (Exhibit 9)				
		DeBenedette, Mark A. et al., "Costimulation of CD28 <sup>+</sup> T Lymphocytes by 4-1BB Ligand," <i>The Journal of Immunology</i> , 1997, 158:551-9. (Exhibit 10)				
		Deeths, Matthew J. and Matthew F. Mescher, "ICAM-1 and B7-1 Provide Similar But Distinct Costimulation For CD28 <sup>+</sup> T Cells, While CD4 <sup>+</sup> Cells are Poorly Costimulated by ICAM-1," <i>Eur. J. Immunol.</i> , 1990, 29:45-53. (Exhibit 11)				
		Dong, Haidong et al., "B7-H1, A Third Member of the B7 Family, Co-Stimulates T-Cell Proliferation and Interleukin-10 Secretion," <i>Nature Medicine</i> , December 1999, 5(12):1365-9. (Exhibit 12)				
		Dubey, Caroline and Michael Croft, "Accessory Molecule Regulation of Naïve CD4 T Cell Activation," <i>Immunologic Research</i> , 1996, 15:114-25. (Exhibit 13)				

EXAMINER	Pitman Gammeter 11/7/02	DATE CONSIDERED
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.		

FORM 1449\*

**INFORMATION DISCLOSURE STATEMENT  
IN AN APPLICATION**

(Use several sheets if necessary)

Docket Number

D0009NP/30436.53USU1

Application Number

09/877,987

Applicant

Robert M. Townsend et al.

Filing Date

June 8, 2001

Group Art Unit

1645

(677)

**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, Etc.)

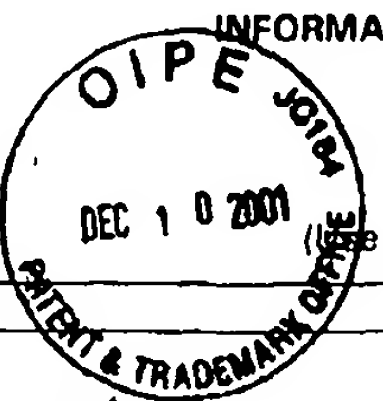
MB	Glysing-Jensen, Troels et al., "Chronic Blockade of CD28-B7-Mediated T-Cell Costimulation by CTLA4Ig Reduces Intimal Thickening in MHC Class I and II Incompatible Mouse Heart Allografts," <i>Transplantation</i> , December 27, 1997, 64(12):1641-5. (Exhibit 14)
	Grabstein, Kenneth H. et al., "The Regulation of T Cell-Dependent Antibody Formation in Vitro by CD40 Ligand and IL-2," <i>The Journal of Immunology</i> , April 15, 1993, 150(8):3141-7. (Exhibit 15)
	Graf, Daniel et al., "Cloning of TRAP, a ligand for CD40 on Human T Cells," <i>Eur. J. Immunol.</i> , 1992, 22:3191-4. (Exhibit 16)
	Green, Jonathan M. and Craig B. Thompson, "Modulation of T Cell Proliferative Responses by Accessory Cell Interactions," <i>Immunologic Research</i> , 1994, 13:3234-43. (Exhibit 17)
	Greenfield, Edward A. et al., "CD28/B7 Costimulation: A Review," <i>Critical Reviews in Immunology</i> , 1998, 18:389-418. (Exhibit 18)
	Griggs, Nathan D. et al., "The Relative Contribution of the CD28 and gp39 Costimulatory Pathways in the Clonal Expression and Pathogenic Acquisition of Self-Reactive T Cells," <i>J. Exp. Med.</i> , March 1996, 183:801-10. (Exhibit 19)
	Hardy, R.R., "Chapter 13: Purification and Characterization of Monoclonal Antibodies," <i>Handbook of Experimental Immunology</i> , 1986, 13.1-13. (Exhibit 20)
	Harper, Katherine et al., "CTLA-4 and CD28 Activated Lymphocyte Molecules are Closely Related in Both Mouse and Human as to Sequence, Message Expression, Gene Structure and Chromosomal Location," <i>The Journal of Immunology</i> , August 1, 1991, 147(3):1037-44. (Exhibit 21)
	Hathcock, Karen S. et al., "Identification of an Alternative CTLA-4 Ligand Costimulatory for T Cell Activation," <i>Science</i> , November 5, 1993, 905-7. (Exhibit 22)
	Hollenbaugh, Diane et al., "The Human T Cell Antigen gp39, a Member of the TNF Gene Family, is a Ligand for the CD40 Receptor: Expression of a Soluble Form of gp39 with B Cell Co-Stimulatory Activity," <i>The EMBO Journal</i> , 1992, 11(12):4313-21. (Exhibit 23)
	Hurtado, Jose C. et al., "Signals Through 4-1BB Are Costimulatory to Previously Activated Splenic T Cells and Inhibit Activation-Induced Cell Death," <i>The Journal of Immunology</i> , 1997, 158:2600-9. (Exhibit 24)
	Hutloff, Andreas et al., "ICOS is an Inducible T-Cell Co-Stimulator Structurally and Functionally Related CD28," <i>Nature</i> , January 1999, 397:263-6. (Exhibit 25)
	Isobe, Mitsuaki et al., "Acceptance of Primary Skin Graft After Treatment with Anti-Intercellular Adhesion Molecule-1 and Anti-Leukocyte Function-Associated Antigen-1 Monoclonal Antibodies in Mice," <i>Transplantation</i> , August 15, 1996, 62(3):411-3. (Exhibit 26)
	Isobe, Mitsuaki et al., "Regulation by Differential Development of Th1 and Th2 Cells in Peripheral Tolerance to Cardiac Allograft Induced by Blocking ICAM-1/LFA-1 Adhesion," <i>Circulation</i> , 1997, 96:2247-53. (Exhibit 27)
	Isobe, Mitsuaki et al., "Specific Acceptance of Cardiac Allograft After Treatment with Antibodies to ICAM-1 and LFA-1," <i>Science</i> , February 1992, 255:1125-7. (Exhibit 28)
	Judge, Thomas A. et al., "The In Vivo Mechanism of Action of CTLA4Ig," <i>The American Association of Immunologists</i> , 1996, 156:2294-9. (Exhibit 29)
PH	Judge, Thomas A. et al., "The Role of CD80, CD86 and CTLA4 in Alloimmune Responses and the Induction of Long-Term Allograft Survival," <i>The American Association of Immunologists</i> , 1999, 162:1947-51. (Exhibit 30)

EXAMINER

PHUUYANG 11/7/02

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

<b>FORM 1449*</b>  <b>INFORMATION DISCLOSURE STATEMENT</b> <b>IN AN APPLICATION</b>  	Docket Number	Application Number
	D0009NP/30436.53USU1	09/877,987
	Applicant	
	Robert M. Townsend et al.	
	Filing Date	Group Art Unit
	June 8, 2001	1645 1644

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
M		June, Carl H. et al., "The B7 and CD28 Receptor Families," <i>Immunology Today</i> , 1994, 15(7):321-31. (Exhibit 31)
		Keizer, Gerrit D. et al., "Biochemical and Functional Characteristics of the Human Leukocyte Membrane Antigen Family LFA-1, Mo-1 and p150,95*," <i>Eur. J. Immunol.</i> , 1985, 15:1142-7. (Exhibit 32)
		Kim, Jong J. et al., "Intracellular Adhesion Molecule-1 Modulates $\beta$ -Chemokines and Directly Costimulates T Cells In Vivo," <i>The Journal of Clinical Investigation</i> , March 1999, 103(6):869-77. (Exhibit 33)
		Kirk, Allan D. et al., "CTLA4-Ig and Anti-CD40 Ligand Prevent Renal Allograft Rejection in Primates," <i>Proc. Nat'l. Acad. Sci. USA</i> , August 1997, 94:8789-94. (Exhibit 34)
		Konieczny, Bogumila T. et al., "IFN- $\gamma$ is Critical for Long-Term Allograft Survival Induced by Blocking the CD28 and CD40 Ligand T Cell Costimulation Pathways," <i>The Journal of Immunology</i> , 1998, 160:2059-64. (Exhibit 35)
		Larsen, Christian P. et al., "CD40-gp39 Interactions Play a Critical Role During Allograft Rejection," <i>Transplantation</i> , January 15, 1996, 61(1):4-9. (Exhibit 36)
		Larsen, Christian P. et al., "Long-Term Acceptance of Skin and Cardiac Allografts After Blocking CD40 and CD28 Pathways," <i>Nature</i> , May 30, 1996, 381:434-8. (Exhibit 37)
		Lenschow, Deborah J. et al., "CD28/B7 System of T Cell Costimulation," <i>Annu. Rev. Immunol.</i> , 1996, 14:233-58. (Exhibit 38)
		Lenschow, Deborah J. et al., "Long-Term Survival of Xenogeneic Pancreatic Islet Grafts Induced by CTLA4Ig," <i>Science</i> , August 7, 1992, 257:789-92. (Exhibit 39)
		Linsley, Peter S. et al., "CTLA-4 is a Second Receptor for the B Cell Activation Antigen B7," <i>J. Exp. Med.</i> , September 1991, 174:561-8. (Exhibit 40)
		Linsley, Peter S. et al., "Immunosuppression in Vivo by a Soluble Form of the CTLA-4 T Cell Activation Molecule," <i>Science</i> , August 7, 1992, 257:792-5. (Exhibit 41)
		Miwa, Shiro et al., "Effect of Anti-Intercellular Adhesion Molecule-1 and Anti-Leukocyte Function Associated Antigen-1 Monoclonal Antibodies on Rat-to-Mouse Cardiac Xenograft Rejection," <i>Surgery</i> , June 1997, 121(6):681-9. (Exhibit 42)
		Ni, Hsiao-Tzu et al., "Signaling Pathways Activated by Leukocyte Function-Associated Ag-1-Dependent Costimulation," <i>The Journal of Immunology</i> , 1999, 162:5183-9. (Exhibit 43)
		Niimi, Masanori et al., "The Role of the CD40 Pathway in Alloantigen-Induced Hyporesponsiveness In Vivo," <i>The Journal of Immunology</i> , 1998, 161:5331-7. (Exhibit 44)
		Russell, Mary E. et al., "Chronic Cardiac Rejection in the LEW to F344 Rat Model Blockade of CD28-B7 Costimulation by CTLA4Ig Modulates T Cell And Macrophage Activation and Attenuates Arteriosclerosis," <i>J. Clin. Invest.</i> , February 1996, 97(3):833-8. (Exhibit 45)
		Shimizu, Yoji et al., "Roles of Adhesion Molecules in T-Cell Recognition: Fundamental Similarities Between Four Integrins on Resting Human T Cells (LFA-1, VLA-4, VLA-5, VLA-6) in Expression, Binding and Costimulation," <i>Immunological Reviews</i> , 1990, 114:109-43. (Exhibit 46)
R		Sun, Hong et al., "Prevention of Chronic Rejection in Mouse Aortic Allografts by Combined Treatment with CTLA4-Ig and Anti-CD40 Ligand Monoclonal Antibody," <i>Transplantation</i> , December 12, 1997, 64(12):1838-56. (Exhibit 47)

EXAMINER	<i>Phuoc Tran</i> 1/14/03	DATE CONSIDERED
EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.		

A circular black and white stamp. The outer ring contains the text "INTELLECTUAL PROPERTY OFFICE" at the bottom and "IPO" at the top. The center of the stamp contains the date "DEC 10 2001".

**INFORMATION DISCLOSURE STATEMENT  
IN AN APPLICATION**

(Use several sheets if necessary)

**Docket Number**

Application Number

D0009NP/30436.53USU1

097877,987

**Applicant**

Robert M. Lowengrub et al.

Filing Date

Group Art Unit

June 8, 2001

1645

5000

**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, Etc.)

[illegible]

EXAMINER

EXAMINER Dikun Namba 11/17/03

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form for next communication to the Applicant.

\*Substitute Disclosure Statement Form (PTO-1449)

Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE